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(54) Title: MUTANT SODIUM CHANNEL NAv1.7 AND METHODS RELATED THERETO

(57) Abstract: Described are mutant Na_v1.7 sodium channel alpha-subunits and nucleic acid sequences encoding such mutants. Further described are methods for characterizing a nucleic acid sequence that encodes a Na_v1 sodium channel alpha-subunit, methods for determining a Na_v1.7 haplotype, methods for determining a subject's predisposition to a neurologic disorder associated with a sodium channel mutation, and methods of identifying a compound that modulates mutant Na_v1.7 sodium channels. Other materials, compositions, articles, devices, and methods relating to mutant Na_v1.7 sodium channels are also described herein.





SEQUENCE LISTING

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Glu Pro Leu Ser Glu Asp Asp Phe Glu Met Phe Tyr Glu Val Trp Glu
      1765 1770 1775
Lys Phe Asp Pro Asp Ala Thr Gln Phe Ile Glu Phe Ser Lys Leu Ser
        1780 1785
Asp Phe Ala Ala Ala Leu Asp Pro Pro Leu Leu Ile Ala Lys Pro Asn
1795 1800 1805
Lys Val Gln Leu Ile Ala Met Asp Leu Pro Met Val Ser Gly Asp Arg
  1810 1815 1820
Ile His Cys Leu Asp Ile Leu Phe Ala Phe Thr Lys Arg Val Leu Gly
1825
               1830 1835 1840
Glu Ser Gly Glu Met Asp Ser Leu Arg Ser Gln Met Glu Glu Arg Phe
           1845 1850 1855
Met Ser Ala Asn Pro Ser Lys Val Ser Tyr Glu Pro Ile Thr Thr
        1860
             1865
                              1870
Leu Lys Arg Lys Gln Glu Asp Val Ser Ala Thr Val Ile Gln Arg Ala
    1875 1880 1885
Tyr Arg Arg Tyr Arg Leu Arg Gln Asn Val Lys Asn Ile Ser Ser Ile
1890 1895 1900
Tyr Ile Lys Asp Gly Asp Arg Asp Asp Leu Leu Asn Lys Lys Asp
1905 1910 1915
Met Ala Phe Asp Asn Val Asn Glu Asn Ser Ser Pro Glu Lys Thr Asp
           1925 1930
Ala Thr Ser Ser Thr Thr Ser Pro Pro Ser Tyr Asp Ser Val Thr Lys
       1940 1945
                                1950
Pro Asp Lys Glu Lys Tyr Glu Gln Asp Arg Thr Glu Lys Glu Asp Lys
    1955 1960 1965
Gly Lys Asp Ser Lys Glu Ser Lys Lys
   1970
                 1975
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<210> 3 <211> 1977 <212> PRT <213> Homo Sapien

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                             25
Lys Glu Pro Lys Glu Glu Lys Lys Asp Asp Asp Glu Glu Ala Pro Lys
       35
                          40
                                            45
Pro Ser Ser Asp Leu Glu Ala Gly Lys Gln Leu Pro Phe Ile Tyr Gly
                    55
                                       60
Asp Ile Pro Pro Gly Met Val Ser Glu Pro Leu Glu Asp Leu Asp Pro
                 70
                                  75
Tyr Tyr Ala Asp Lys Lys Thr Phe Ile Val Leu Asn Lys Gly Lys Thr
                                90
Ile Phe Arg Phe Asn Ala Thr Pro Ala Leu Tyr Met Leu Ser Pro Phe
          100
                             105
                                               110
Ser Pro Leu Arg Arg Ile Ser Ile Lys Ile Leu Val His Ser Leu Phe
  115
                         120
                                          125
Ser Met Leu Ile Met Cys Thr Ile Leu Thr Asn Cys Ile Phe Met Thr
                   135
                               140
Met Asn Asn Pro Gln Asp Trp Thr Lys Asn Val Glu Tyr Thr Phe Thr
145
                           155
                  150
Gly Ile Tyr Thr Phe Glu Ser Leu Val Lys Ile Leu Ala Arg Gly Phe
                               170
                                                   175
Cys Val Gly Glu Phe Thr Phe Leu Arg Asp Pro Trp Asn Trp Leu Asp
            180
                      185
Phe Val Val Ile Val Phe Ala Tyr Leu Thr Glu Phe Val Asn Leu Gly
                   200
                                          205
Asn Val Ser Ala Leu Arg Thr Phe Arg Val Leu Arg Ala Leu Lys Thr
210 215 220
                                         220
Ile Ser Val Ile Pro Gly Leu Lys Thr Ile Val Gly Ala Leu Ile Gln 225 230 235 240
        230
                                    235
Ser Val Lys Lys Leu Ser Asp Val Met Ile Leu Thr Val Phe Cys Leu
             245
                                250
Ser Val Phe Ala Leu Ile Gly Leu Gln Leu Phe Met Gly Asn Leu Lys
        260
                             265
                                                270
His Lys Cys Phe Arg Asn Ser Leu Glu Asn Asn Glu Thr Leu Glu Ser
      275
                       280
                                       285
Ile Met Asn Thr Leu Glu Ser Glu Glu Asp Phe Arg Lys Tyr Phe Tyr
                      295
                                         300
Tyr Leu Glu Gly Ser Lys Asp Ala Leu Leu Cys Gly Phe Ser Thr Asp
                 310
                                   315
Ser Gly Gln Cys Pro Glu Gly Tyr Thr Cys Val Lys Ile Gly Arg Asn
              325
                                 330
                                                    335
Pro Asp Tyr Gly Tyr Thr Ser Phe Asp Thr Phe Ser Trp Ala Phe Leu
         340
                            345
                                                350
Ala Leu Phe Arg Leu Met Thr Gln Asp Tyr Trp Glu Asn Leu Tyr Gln
       355
                       360
Gln Thr Leu Arg Ala Ala Gly Lys Thr Tyr Met Ile Phe Phe Val Val 370 375 380
                      375
                                        380
Val Ile Phe Leu Gly Ser Phe Tyr Leu Ile Asn Leu Ile Leu Ala Val
                 390
                                   395
Val Ala Met Ala Tyr Glu Glu Gln Asn Gln Ala Asn Ile Glu Glu Ala
             405
                                410
                                                   415
Lys Gln Lys Glu Leu Glu Phe Gln Gln Met Leu Asp Arg Leu Lys Lys
                             425
                                                430
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Glu Gln Glu Glu Ala Glu Ala Ile Ala Ala Ala Ala Ala Glu Tyr Thr
                          440
                                   445
Ser Ile Arg Arg Ser Arg Ile Met Gly Leu Ser Glu Ser Ser Ser Glu
                      455
                                          460
Thr Ser Lys Leu Ser Ser Lys Ser Ala Lys Glu Arg Arg Asn Arg Arg
                  470
                                      475
Lys Lys Lys Asn Gln Lys Lys Leu Ser Ser Gly Glu Glu Lys Gly Asp
          485
                                  490
                                                     495
Ala Glu Lys Leu Ser Lys Ser Glu Ser Glu Asp Ser Ile Arg Arg Lys
           500
                             505
                                                510
Ser Phe His Leu Gly Val Glu Gly His Arg Arg Ala His Glu Lys Arg
                           520
                                          525
Leu Ser Thr Pro Asn Gln Ser Pro Leu Ser Ile Arg Gly Ser Leu Phe
                     535
                                         540
Ser Ala Arg Arg Ser Ser Arg Thr Ser Leu Phe Ser Phe Lys Gly Arg
                550
                                     555
Gly Arg Asp Ile Gly Ser Glu Thr Glu Phe Ala Asp Asp Glu His Ser
            565
                                570
Ile Phe Gly Asp Asn Glu Ser Arg Arg Gly Ser Leu Phe Val Pro His
           580
                             585
Arg Pro Gln Glu Arg Arg Ser Ser Asn Ile Ser Gln Ala Ser Arg Ser
       595
                           600
                                              605
Pro Pro Met Leu Pro Val Asn Gly Lys Met His Ser Ala Val Asp Cys
                     615
                                         620
Asn Gly Val Val Ser Leu Val Asp Gly Arg Ser Ala Leu Met Leu Pro
                  630
                                     635
Asn Gly Gln Leu Leu Pro Glu Gly Thr Thr Asn Gln Ile His Lys Lys
              645
                                650
                                                    655
Arg Arg Cys Ser Ser Tyr Leu Leu Ser Glu Asp Met Leu Asn Asp Pro
           660
                              665
                                                 670
Asn Leu Arg Gln Arg Ala Met Ser Arg Ala Ser Ile Leu Thr Asn Thr
      675
                         680
                                              685
Val Glu Glu Leu Glu Glu Ser Arg Gln Lys Cys Pro Pro Trp Trp Tyr
                      695
                                         700
Arg Phe Ala His Lys Phe Leu Ile Trp Asn Cys Ser Pro Tyr Trp Ile
        710
                                   715
Lys Phe Lys Lys Cys Ile Tyr Phe Ile Val Met Asp Pro Phe Val Asp
               725
                                 730
Leu Ala Ile Thr Ile Cys Ile Val Leu Asn Thr Leu Phe Met Ala Met
           740
                              745
Glu His His Pro Met Thr Glu Glu Phe Lys Asn Val Leu Ala Ile Gly
       755
                          760
                                             765
Asn Leu Val Phe Thr Gly Ile Phe Ala Ala Glu Met Val Leu Lys Leu
   770
                      775
                                         780
Ile Ala Met Asp Pro Tyr Glu Tyr Phe Gln Val Gly Trp Asn Ile Phe
                790
                                    795
Asp Ser Leu Ile Val Thr Leu Ser Leu Val Glu Leu Phe Leu Ala Asp
              805
                                810
Val Glu Gly Leu Ser Val Leu Arg Ser Phe Arg Leu Leu Arg Val Phe
          820
                              825
Lys Leu Ala Lys Ser Trp Pro Thr Leu Asn Met Leu Ile Lys Ile Ile
      835
                                           845
                         840
Gly Asn Ser Val Gly Ala Leu Gly Asn Leu Thr Leu Val Leu Ala Ile
  850
                      855
                                        860
Ile Val Phe Ile Phe Ala Val Val Gly Met Gln Leu Phe Gly Lys Ser
                                     875
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Tyr Lys Glu Cys Val Cys Lys Ile Asn Asp Asp Cys Thr Leu Pro Arg
                 890
Trp His Met Asn Asp Phe Phe His Ser Phe Leu Ile Val Phe Arg Val
        900
                        905
Leu Cys Gly Glu Trp Ile Glu Thr Met Trp Asp Cys Met Glu Val Ala
     915
                     920
Gly Gln Ala Met Cys Leu Ile Val Tyr Met Met Val Met Val Ile Gly
                935
                                940
Asn Leu Val Val Leu Asn Leu Phe Leu Ala Leu Leu Leu Ser Ser Phe
             950
                       955
Ser Ser Asp Asn Leu Thr Ala Ile Glu Glu Asp Pro Asp Ala Asn Asn
           965 970
                                         975
Leu Gln Ile Ala Val Thr Arg Ile Lys Lys Gly Ile Asn Tyr Val Lys
        980
                        985
                                       990
Gln Thr Leu Arg Glu Phe Ile Leu Lys Ala Phe Ser Lys Lys Pro Lys
    995
                     1000
                                    1005
Ile Ser Arg Glu Ile Arg Gln Ala Glu Asp Leu Asn Thr Lys Lys Glu
 1010 1015
                                 1020
Asn Tyr Ile Ser Asn His Thr Leu Ala Glu Met Ser Lys Gly His Asn
1025
      1030 1035 1040
Phe Leu Lys Glu Lys Asp Lys Ile Ser Gly Phe Gly Ser Ser Val Asp
            1045
                 1050 1055
Lys His Leu Met Glu Asp Ser Asp Gly Gln Ser Phe Ile His Asn Pro
        1060
              1065 1070
Ser Leu Thr Val Thr Val Pro Ile Ala Pro Gly Glu Ser Asp Leu Glu
     1075
             1080 1085
Asn Met Asn Ala Glu Glu Leu Ser Ser Asp Ser Asp Ser Glu Tyr Ser
  1090 1095 1100
Lys Val Arg Leu Asn Arg Ser Ser Ser Ser Glu Cys Ser Thr Val Asp
      1110 1115
Asn Pro Leu Pro Gly Glu Gly Glu Ala Glu Ala Glu Pro Met Asn
       1125
                          1130
                                           1135
Ser Asp Glu Pro Glu Ala Cys Phe Thr Asp Gly Cys Val Arg Arg Phe
       1140 1145
                                      1150
Ser Cys Cys Gln Val Asn Ile Glu Ser Gly Lys Gly Lys Ile Trp Trp
    1155 1160
                                    1165
Asn Ile Arg Lys Thr Cys Tyr Lys Ile Val Glu His Ser Trp Phe Glu
  1170 1175 1180
Ser Phe Ile Val Leu Met Ile Leu Leu Ser Ser Gly Ala Leu Ala Phe
1185 1190 1195 1200
Glu Asp Ile Tyr Ile Glu Arg Lys Lys Thr Ile Lys Ile Ile Leu Glu
           1205 1210
Tyr Ala Asp Lys Ile Phe Thr Tyr Ile Phe Ile Leu Glu Met Leu Leu
        1220 1225
                                       1230
Lys Trp Ile Ala Tyr Gly Tyr Lys Thr Tyr Phe Thr Asn Ala Trp Cys
     1235 1240
                              1245
Trp Leu Asp Phe Leu Ile Val Asp Val Ser Leu Val Thr Leu Val Ala
  1250 1255 1260
Asn Thr Leu Gly Tyr Ser Asp Leu Gly Pro Ile Lys Ser Leu Arg Thr
               1270
                             1275
Leu Arg Ala Leu Arg Pro Leu Arg Ala Leu Ser Arg Phe Glu Gly Met
           1285
                          1290
                                           1295
Arg Val Val Asn Ala Leu Ile Gly Ala Ile Pro Ser Ile Met Asn
        1300 1305 1310
Val Leu Leu Val Cys Leu Ile Phe Trp Leu Ile Phe Ser Ile Met Gly
             1320
                                     1325
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Val Asn Leu Phe Ala Gly Lys Phe Tyr Glu Cys Ile Asn Thr Thr Asp
        1335 1340
Gly Ser Arg Phe Pro Ala Ser Gln Val Pro Asn Arg Ser Glu Cys Phe
       1350
                      1355
Ala Leu Met Asn Val Ser Gln Asn Val Arg Trp Lys Asn Leu Lys Val
           1365 1370
                                          1375
Asn Phe Asp Asn Val Gly Leu Gly Tyr Leu Ser Leu Leu Gln Val Ala
        1380
                        1385
                                       1390
Thr Phe Lys Gly Trp Thr Ile Ile Met Tyr Ala Ala Val Asp Ser Val
     1395
              1400
                             1405
Asn Val Asp Lys Gln Pro Lys Tyr Glu Tyr Ser Leu Tyr Met Tyr Ile
                 1415
                         1420
Tyr Phe Val Val Phe Ile Ile Phe Gly Ser Phe Phe Thr Leu Asn Leu
             1430 1435
Phe Ile Gly Val Ile Ile Asp Asn Phe Asn Gln Gln Lys Lys Leu
          1445 1450
Gly Gly Gln Asp Ile Phe Met Thr Glu Glu Gln Lys Lys Tyr Tyr Asn
       1460 1465
                             1470
Ala Met Lys Lys Leu Gly Ser Lys Lys Pro Gln Lys Pro Ile Pro Arg
     1475 1480 1485
Pro Gly Asn Lys Ile Gln Gly Cys Ile Phe Asp Leu Val Thr Asn Gln
   1490 1495
                         1500
Ala Phe Asp Ile Ser Ile Met Val Leu Ile Cys Leu Asn Met Val Thr
                             1515
        1510
                                              1520
Met Met Val Glu Lys Glu Gly Gln Ser Gln His Met Thr Glu Val Leu
           1525
                   1530
                                           1535
Tyr Trp Ile Asn Val Val Phe Ile Ile Leu Phe Thr Gly Glu Cys Val
       1540
                1545
                                       1550
Leu Lys Leu Ile Ser Leu Arg His Tyr Tyr Phe Thr Val Gly Trp Asn
      1555 1560 1565
Ile Phe Asp Phe Val Val Ile Ile Ser Ile Val Gly Met Phe Leu
                 1575
                                 1580
Ala Asp Leu Ile Glu Thr Tyr Phe Val Ser Pro Thr Leu Phe Arg Val
              1590
                              1595
Ile Arg Leu Ala Arg Ile Gly Arg Ile Leu Arg Leu Val Lys Gly Ala
          1605
                         1610 1615
Lys Gly Ile Arg Thr Leu Leu Phe Ala Leu Met Met Ser Leu Pro Ala
        1620
              1625 1630
Leu Phe Asn Ile Gly Leu Leu Leu Phe Leu Val Met Phe Ile Tyr Ala
      1635 1640 1645
Ile Phe Gly Met Ser Asn Phe Ala Tyr Val Lys Lys Glu Asp Gly Ile
                1655
                                 1660
Asn Asp Met Phe Asn Phe Glu Thr Phe Gly Asn Ser Met Ile Cys Leu
            1670
                              1675
Phe Gln Ile Thr Thr Ser Ala Gly Trp Asp Gly Leu Leu Ala Pro Ile
         1685 1690
                                           1695
Leu Asn Ser Lys Pro Pro Asp Cys Asp Pro Lys Lys Val His Pro Gly
        1700 1705
                               1710
Ser Ser Val Glu Gly Asp Cys Gly Asn Pro Ser Val Gly Ile Phe Tyr
     1715
                     1720
                                     1725
Phe Val Ser Tyr Ile Ile Ile Ser Phe Leu Val Val Val Asn Met Tyr
  1730
                 1735
                                1740
Ile Ala Val Ile Leu Glu Asn Phe Ser Val Ala Thr Glu Glu Ser Thr
              1750 1755
Glu Pro Leu Ser Glu Asp Asp Phe Glu Met Phe Tyr Glu Val Trp Glu
            1765
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1770

1775

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Lys Phe Asp Pro Asp Ala Thr Gln Phe Ile Glu Phe Ser Lys Leu Ser
        1780 1785 1790
Asp Phe Ala Ala Ala Leu Asp Pro Pro Leu Leu Ile Ala Lys Pro Asn
     1795
                     1800
                                      1805
Lys Val Gln Leu Ile Ala Met Asp Leu Pro Met Val Ser Gly Asp Arg
  1810
                  1815
                                 1820
Ile His Cys Leu Asp Ile Leu Phe Ala Phe Thr Lys Arg Val Leu Gly
1825
               1830 1835
Glu Ser Gly Glu Met Asp Ser Leu Arg Ser Gln Met Glu Glu Arg Phe
          1845 1850 1855
Met Ser Ala Asn Pro Ser Lys Val Ser Tyr Glu Pro Ile Thr Thr
        1860 1865
                                        1870
Leu Lys Arg Lys Gln Glu Asp Val Ser Ala Thr Val Ile Gln Arg Ala
1875 1880 1885
     1875 1880
Tyr Arg Arg Tyr Arg Leu Arg Gln Asn Val Lys Asn Ile Ser Ser Ile
 1890 1895
                                1900
Tyr Ile Lys Asp Gly Asp Arg Asp Asp Asp Leu Leu Asn Lys Lys Asp
1905 1910 1915 192
                                               1920
Met Ala Phe Asp Asn Val Asn Glu Asn Ser Ser Pro Glu Lys Thr Asp
           1925 1930 1935
Ala Thr Ser Ser Thr Thr Ser Pro Pro Ser Tyr Asp Ser Val Thr Lys
       1940 1945 1950
Pro Asp Lys Glu Lys Tyr Glu Gln Asp Arg Thr Glu Lys Glu Asp Lys
     1955 1960
                                     1965
Gly Lys Asp Ser Lys Glu Ser Lys Lys
                  1975
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165
                                   170
Cys Val Gly Glu Phe Thr Phe Leu Arg Asp Pro Trp Asn Trp Leu Asp
                       185
           180
                                                   190
Phe Val Val Ile Val Phe Ala Tyr Leu Thr Glu Phe Val Asn Leu Gly
                           200
                                    205
Asn Val Ser Ala Leu Arg Thr Phe Arg Val Leu Arg Ala Leu Lys Thr
                      215
                                          220
Ile Ser Val Ile Pro Gly Leu Lys Thr Ile Val Gly Ala Leu Ile Gln 225 230 235 240
Ser Val Lys Lys Leu Ser Asp Val Met Ile Leu Thr Val Phe Cys Leu 245 250 255
Ser Val Phe Ala Leu Ile Gly Leu Gln Leu Phe Met Gly Asn Leu Lys
           260
                               265
His Lys Cys Phe Arg Asn Ser Leu Glu Asn Asn Glu Thr Leu Glu Ser
       275
                          280
                                             285
Ile Met Asn Thr Leu Glu Ser Glu Glu Asp Phe Arg Lys Tyr Phe Tyr
                     295
                                        300
Tyr Leu Glu Gly Ser Lys Asp Ala Leu Leu Cys Gly Phe Ser Thr Asp 305 310 315 320
Ser Gly Gln Cys Pro Glu Gly Tyr Thr Cys Val Lys Ile Gly Arg Asn
325 330 335
                               330
                                                     335
Pro Asp Tyr Gly Tyr Thr Ser Phe Asp Thr Phe Ser Trp Ala Phe Leu 340 345 350
                               345
                                                   350
Ala Leu Phe Arg Leu Met Thr Gln Asp Tyr Trp Glu Asn Leu Tyr Gln
      355
                          360
                                              365
Gln Thr Leu Arg Ala Ala Gly Lys Thr Tyr Met Ile Phe Phe Val Val
                    375
                                           380
Val Ile Phe Leu Gly Ser Phe Tyr Leu Ile Asn Leu Ile Leu Ala Val
385
                  390
                                      395
Val Ala Met Ala Tyr Glu Glu Gln Asn Gln Ala Asn Ile Glu Glu Ala
               405
                                  410
Lys Gln Lys Glu Leu Glu Phe Gln Gln Met Leu Asp Arg Leu Lys Lys
          420
                              425
                                                  430
Glu Gln Glu Glu Ala Glu Ala Ile Ala Ala Ala Ala Glu Tyr Thr
       435
                          440
                                             445
Ser Ile Arg Arg Ser Arg Ile Met Gly Leu Ser Glu Ser Ser Ser Glu
  450 455
                                        460
Thr Ser Lys Leu Ser Ser Lys Ser Ala Lys Glu Arg Arg Asn Arg Arg 465 470 475 480
Lys Lys Lys Asn Gln Lys Lys Leu Ser Ser Gly Glu Glu Lys Gly Asp
                                  490
Ala Glu Lys Leu Ser Lys Ser Glu Ser Glu Asp Ser Ile Arg Arg Lys
          500
                              505
Ser Phe His Leu Gly Val Glu Gly His Arg Arg Ala His Glu Lys Arg
     515
                          520
                                              525
Leu Ser Thr Pro Asn Gln Ser Pro Leu Ser Ile Arg Gly Ser Leu Phe
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                                        540
Ser Ala Arg Arg Ser Ser Arg Thr Ser Leu Phe Ser Phe Lys Gly Arg 545 550 560
Gly Arg Asp Ile Gly Ser Glu Thr Glu Phe Ala Asp Asp Glu His Ser
                    570
              565
Ile Phe Gly Asp Asn Glu Ser Arg Arg Gly Ser Leu Phe Val Pro His
           580
                              585
                                               590
Arg Pro Gln Glu Arg Arg Ser Ser Asn Ile Ser Gln Ala Ser Arg Ser
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                  600
Pro Pro Met Leu Pro Val Asn Gly Lys Met His Ser Ala Val Asp Cys
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610
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Asn Gly Val Val Ser Leu Val Asp Gly Arg Ser Ala Leu Met Leu Pro
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                  630
                                    635
Tyr Gly Gln Leu Leu Pro Glu Gly Thr Thr Asn Gln Ile His Lys Lys
               645
                               650
Arg Arg Cys Ser Ser Tyr Leu Leu Ser Glu Asp Met Leu Asn Asp Pro
          660
                          665
                                               670
Asn Leu Arg Gln Arg Ala Met Ser Arg Ala Ser Ile Leu Thr Asn Thr
     675
               680
                                          685
Val Glu Glu Leu Glu Glu Ser Arg Gln Lys Cys Pro Pro Trp Trp Tyr
           695
                                       700
Arg Phe Ala His Lys Phe Leu Ile Trp Asn Cys Ser Pro Tyr Trp Ile
                  710
                                    715
Lys Phe Lys Lys Cys Ile Tyr Phe Ile Val Met Asp Pro Phe Val Asp
              725
                                730
Leu Ala Ile Thr Ile Cys Ile Val Leu Asn Thr Leu Phe Met Ala Met
           740
                             745
                                             750
Glu His His Pro Met Thr Glu Glu Phe Lys Asn Val Leu Ala Ile Gly
                      760
                                   765
Asn Leu Val Phe Thr Gly Ile Phe Ala Ala Glu Met Val Leu Lys Leu
                     775
                               780
Ile Ala Met Asp Pro Tyr Glu Tyr Phe Gln Val Gly Trp Asn Ile Phe
               790
                                    795
Asp Ser Leu Ile Val Thr Leu Ser Leu Val Glu Leu Phe Leu Ala Asp
             805
                                810
Val Glu Gly Leu Ser Val Leu Arg Ser Phe Arg Leu Leu Arg Val Phe
          820
                            825
Lys Leu Ala Lys Ser Trp Pro Thr Leu Asn Met Leu Ile Lys Ile Ile
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Gly Asn Ser Val Gly Ala Leu Gly Asn Leu Thr Leu Val Leu Ala Ile
                      855
Ile Val Phe Ile Phe Ala Val Val Gly Met Gln Leu Phe Gly Lys Ser
                 870
                                  875
Tyr Lys Glu Cys Val Cys Lys Ile Asn Asp Asp Cys Thr Leu Pro Arg
              885
                               890
                                                  895
Trp His Met Asn Asp Phe Phe His Ser Phe Leu Ile Val Phe Arg Val
         900
                          905
                                              910
Leu Cys Gly Glu Trp Ile Glu Thr Met Trp Asp Cys Met Glu Val Ala
       915
                      920
                                           925
Gly Gln Ala Met Cys Leu Ile Val Tyr Met Met Val Met Val Ile Gly
   930 935
                                        940
Asn Leu Val Val Leu Asn Leu Phe Leu Ala Leu Leu Ser Ser Phe
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                                    955
Ser Ser Asp Asn Leu Thr Ala Ile Glu Glu Asp Pro Asp Ala Asn Asn
           965
                                970
Leu Gln Ile Ala Val Thr Arg Ile Lys Lys Gly Ile Asn Tyr Val Lys
          980
                           985
                                      990
Gln Thr Leu Arg Glu Phe Ile Leu Lys Ala Phe Ser Lys Lys Pro Lys
                         1000
                                 1005
Ile Ser Arg Glu Ile Arg Gln Ala Glu Asp Leu Asn Thr Lys Lys Glu
                     1015
                                       1020
Asn Tyr Ile Ser Asn His Thr Leu Ala Glu Met Ser Lys Gly His Asn
1025
     1030
                                   1035
Phe Leu Lys Glu Lys Asp Lys Ile Ser Gly Phe Gly Ser Ser Val Asp
1045 1050 1055
Lys His Leu Met Glu Asp Ser Asp Gly Gln Ser Phe Ile His Asn Pro
```

			100	_				100	-					_	
C	*	m\	1060		**- 1	_		106	-			_	1070		
	Leu	1075	5				1080)				108	5		
Asn	Met 1090	Asn)	Ala	Glu	Glu	Leu 1095		Ser	Asp	Ser	Asp 1100		Glu	Tyr	Ser
Lys	Val	Arq	Leu	Asn	Ara	Ser	Ser	Ser	Ser	Glu	Cvs	Ser	Thr	Val	Asp
1109	5	_			111(1115					1120
	Pro	T.011	Dro	Glv			C1	C1	71-			C1	Dwa	M-+	
				1125	5				1130	0				113	5
Ser	Asp	Glu	Pro 1140		Ala	Суѕ	Phe	Thr 1145		Gly	Cys	Val	Arg 1150		Phe
Ser	Cys	Cys 1155	Gln	Val	Asn	Ile	Glu 1160		Gly	Lys	Gly	Lys 1165	Ile		Trp
Asn	Ile 1170	Arg		Thr	Cys	Tyr 1175	Lys		Val	Glu		Ser		Phe	Glu
Ser	Phe		Val	T.e.u	Met			Len	Ser	Sor	1180		T OU	λl 5	Pho
1185	5		- 41		1190		u	J. G. U.	OCT	1195		лта	⊐∈ u	viq	1200
	Asp	Tle	Tur	Tla			T.v.0	T.370	ጥ _ኮ ∽			T10	T10	Low	
				1205	5				1210)				1215	5
	Ala		1220)				1225	5				1230)	
Lys	Trp	Ile 1235		Tyr	Gly	Tyr	Lys 1240		Tyr	Phe	Thr	Asn 1245		Trp	Суѕ
Trp	Leu 1250		Phe	Leu	Ile	Val 1255	Asp		Ser	Leu	Val 1260	Thr		Val	Ala
Asn	Thr		Gly	Tyr	Ser			Glv	Pro	Ile			Leu	Arg	Thr
1265	5				1270)				1275	5				1280
	Arg			1285	5				1290)				1295	5
	Val		1300)				1305	5				1310)	
Val	Leu	Leu 1315		Cys	Leu	Ile	Phe 1320		Leu	Ile	Phe	Ser 1325	Ile		Gly
Val	Asn 1330	Leu		Ala	Gly	Lys 1335	Phe		Glu	Cys	Ile 1340	Asn		Thr	Asp
Gly 1345	Ser		Phe	Pro	Ala 1350	Ser		Val	Pro	Asn 1355	Arg		Glu	Cys	
	Leu	Met	Asn	Val			Aen	۷al	Δτα			Δος	Len	Luc	1360
				1365	•				1370)				1375	5
Asn	Phe	Asp			Gly	Leu	Gly			Ser	Leu	Leu			Ala
mъ	Dk -	T	1380			-1		1385					1390		
	Phe	1395	i				1400)				1405	i		
Asn	Val	Asp	Lys	Gln	Pro	Lys	Tyr	Glu	Tyr	Ser	Leu			Tyr	Ile
	1410	1				1415	,				1420				
	Phe	Val	Val	Phe	Ile	Ile	Phe	Gly	Ser	Phe	Phe	Thr	Leu	Asn	Leu
1425	5				1430)				1435	j				1440
Phe	Ile	Gly	Val	Ile 1445	Ile	Asp	Asn	Phe	Asn 1450	Gln	Gln	Lys	Lys	Lys 1455	Leu
Glv	Gly	Gln	asA			Met	Thr	Glu			Lvs	Lvs	Tvr		
			1460					1465			-10	_,,	1470		
Ala	Met	Lys 1475	Lys		Gly		Lys	Lys		Gln			Ile		Arg
Pro				т1 -	C1 ~		1480		Db ~	7.00		1485		7.0-	C1-
	Gly 1490					1495	i				1500				
Ala	Phe	Asp	Ile	Ser	Ile	Met	Val	Leu	Ile	Cys	Leu	Asn	Met	Val	Thr

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1505
               1510
                               1515
Met Met Val Glu Lys Glu Gly Gln Ser Gln His Met Thr Glu Val Leu
                    1530
            1525
                                    1535
Tyr Trp Ile Asn Val Val Phe Ile Ile Leu Phe Thr Gly Glu Cys Val
         1540 1545
                                        1550
Leu Lys Leu Ile Ser Leu Arg His Tyr Tyr Phe Thr Val Gly Trp Asn
     1555 1560
                           1565
Ile Phe Asp Phe Val Val Val Ile Ile Ser Ile Val Gly Met Phe Leu
  1570 1575 1580
Ala Asp Leu Ile Glu Thr Tyr Phe Val Ser Pro Thr Leu Phe Arg Val
1585 1590 1595 1600
Ile Arg Leu Ala Arg Ile Gly Arg Ile Leu Arg Leu Val Lys Gly Ala
            1605
                            1610
                                           1615
Lys Gly Ile Arg Thr Leu Leu Phe Ala Leu Met Met Ser Leu Pro Ala
         1620
              1625 1630
Leu Phe Asn Ile Gly Leu Leu Leu Phe Leu Val Met Phe Ile Tyr Ala
     1635
                    1640 1645
Ile Phe Gly Met Ser Asn Phe Ala Tyr Val Lys Lys Glu Asp Gly Ile
                           1660
  1650 1655
Asn Asp Met Phe Asn Phe Glu Thr Phe Gly Asn Ser Met Ile Cys Leu
              1670 1675
Phe Gln Ile Thr Thr Ser Ala Gly Trp Asp Gly Leu Leu Ala Pro Ile
          1685 1690
Leu Asn Ser Lys Pro Pro Asp Cys Asp Pro Lys Lys Val His Pro Gly
        1700 1705
Ser Ser Val Glu Gly Asp Cys Gly Asn Pro Ser Val Gly Ile Phe Tyr
1715 1720 1725
Phe Val Ser Tyr Ile Ile Ile Ser Phe Leu Val Val Val Asn Met Tyr
  1730 1735 1740
Ile Ala Val Ile Leu Glu Asn Phe Ser Val Ala Thr Glu Glu Ser Thr
1745
               1750
                              1755 1760
Glu Pro Leu Ser Glu Asp Asp Phe Glu Met Phe Tyr Glu Val Trp Glu
           1765 1770
                                          1775
Lys Phe Asp Pro Asp Ala Thr Gln Phe Ile Glu Phe Ser Lys Leu Ser
        1780 1785 1790
Asp Phe Ala Ala Ala Leu Asp Pro Pro Leu Leu Ile Ala Lys Pro Asn
     1795 1800 1805
Lys Val Gln Leu Ile Ala Met Asp Leu Pro Met Val Ser Gly Asp Arg
   1810 1815 1820
Ile His Cys Leu Asp Ile Leu Phe Ala Phe Thr Lys Arg Val Leu Gly
               1830 1835
Glu Ser Gly Glu Met Asp Ser Leu Arg Ser Gln Met Glu Glu Arg Phe 1845 1850 1855
Met Ser Ala Asn Pro Ser Lys Val Ser Tyr Glu Pro Ile Thr Thr
        1860 1865
                                        1870
Leu Lys Arg Lys Gln Glu Asp Val Ser Ala Thr Val Ile Gln Arg Ala
     1875 1880 1885
Tyr Arg Arg Tyr Arg Leu Arg Gln Asn Val Lys Asn Ile Ser Ser Ile
1890 1895 1900
Tyr Ile Lys Asp Gly Asp Arg Asp Asp Leu Leu Asn Lys Lys Asp
1905 1910 1915
Met Ala Phe Asp Asn Val Asn Glu Asn Ser Ser Pro Glu Lys Thr Asp
            1925
                           1930
Ala Thr Ser Ser Thr Thr Ser Pro Pro Ser Tyr Asp Ser Val Thr Lys
1940 1945 1950
Pro Asp Lys Glu Lys Tyr Glu Gln Asp Arg Thr Glu Lys Glu Asp Lys
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1955 1960 1965 Gly Lys Asp Ser Lys Glu Ser Lys Lys 1970 1975

<210> 5 <211> 1977 <212> PRT <213> Homo Sapien

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Ala Leu Phe Arg Leu Met Thr Gln Asp Tyr Trp Glu Asn Leu Tyr Gln
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                                             365
Gln Thr Leu Arg Ala Ala Gly Lys Thr Tyr Met Ile Phe Phe Val Val
                   375
                                         380
Val Ile Phe Leu Gly Ser Phe Tyr Leu Ile Asn Leu Ile Leu Ala Val
                  390
                                    395
Val Ala Met Ala Tyr Glu Glu Gln Asn Gln Ala Asn Ile Glu Glu Ala
             405
                                 410
Lys Gln Lys Glu Leu Glu Phe Gln Gln Met Leu Asp Arg Leu Lys Lys
          420
                            425
                                               430
Glu Gln Glu Glu Ala Glu Ala Ile Ala Ala Ala Ala Ala Glu Tyr Thr
                        440
                                           445
Ser Ile Arg Arg Ser Arg Ile Met Gly Leu Ser Glu Ser Ser Ser Glu
                   455
                                         460
Thr Ser Lys Leu Ser Ser Lys Ser Ala Lys Glu Arg Arg Asn Arg Arg
                 470
                                    475
Lys Lys Lys Asn Gln Lys Lys Leu Ser Ser Gly Glu Glu Lys Gly Asp
          485
                         490
Ala Glu Lys Leu Ser Lys Ser Glu Ser Glu Asp Ser Ile Arg Arg Lys
          500
                   505
Ser Phe His Leu Gly Val Glu Gly His Arg Arg Ala His Glu Lys Arg
       515
                          520
                                          525
Leu Ser Thr Pro Asn Gln Ser Pro Leu Ser Ile Arg Gly Ser Leu Phe
                    535
                                       540
Ser Ala Arg Arg Ser Ser Arg Thr Ser Leu Phe Ser Phe Lys Gly Arg
               550
                                   555
Gly Arg Asp Ile Gly Ser Glu Thr Glu Phe Ala Asp Asp Glu His Ser
            565
                        570
                                                    575
Ile Phe Gly Asp Asn Glu Ser Arg Arg Gly Ser Leu Phe Val Pro His
           580
                             585
                                             590
Arg Pro Gln Glu Arg Arg Ser Ser Asn Ile Ser Gln Ala Ser Arg Ser
                        600
                                             605
Pro Pro Met Leu Pro Val Asn Gly Lys Met His Ser Ala Val Asp Cys
                   615
                                        620
Asn Gly Val Val Ser Leu Val Asp Gly Arg Ser Ala Leu Met Leu Pro
            630
                                     635
Asn Gly Gln Leu Leu Pro Glu Gly Thr Thr Asn Gln Ile His Arg Lys
              645
                              650
Arg Arg Cys Ser Ser Tyr Leu Leu Ser Glu Asp Met Leu Asn Asp Pro
           660
                              665
                                             670
Asn Leu Arg Gln Arg Ala Met Ser Arg Ala Ser Ile Leu Thr Asn Thr
                        680
                                           685
Val Glu Glu Leu Glu Glu Ser Arg Gln Lys Cys Pro Pro Trp Trp Tyr
                     695
                                         700
Arg Phe Ala His Lys Phe Leu Ile Trp Asn Cys Ser Pro Tyr Trp Ile
        710
                                 715
Lys Phe Lys Lys Cys Ile Tyr Phe Ile Val Met Asp Pro Phe Val Asp 725 730 735
Leu Ala Ile Thr Ile Cys Ile Val Leu Asn Thr Leu Phe Met Ala Met
          740
                             745
Glu His His Pro Met Thr Glu Glu Phe Lys Asn Val Leu Ala Ile Gly
       755
                          760
                                            765
Asn Leu Val Phe Thr Gly Ile Phe Ala Ala Glu Met Val Leu Lys Leu
                      775
                                       780
Ile Ala Met Asp Pro Tyr Glu Tyr Phe Gln Val Gly Trp Asn Ile Phe
                  790
                                   795
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Asp Ser Leu Ile Val Thr Leu Ser Leu Val Glu Leu Phe Leu Ala Asp
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                   810
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Val Glu Gly Leu Ser Val Leu Arg Ser Phe Arg Leu Leu Arg Val Phe
          820
                            825
                                              830
Lys Leu Ala Lys Ser Trp Pro Thr Leu Asn Met Leu Ile Lys Ile Ile
     835
                        840
Gly Asn Ser Val Gly Ala Leu Gly Asn Leu Thr Leu Val Leu Ala Ile
   850
                     855
                                      860
Ile Val Phe Ile Phe Ala Val Val Gly Met Gln Leu Phe Gly Lys Ser
                870
                                875
Tyr Lys Glu Cys Val Cys Lys Ile Asn Asp Asp Cys Thr Leu Pro Arg
885 890 895
             885
                                                 895
Trp His Met Asn Asp Phe Phe His Ser Phe Leu Ile Val Phe Arg Val
         900
                            905
                                              910
Leu Cys Gly Glu Trp Ile Glu Thr Met Trp Asp Cys Met Glu Val Ala
     915
                        920
                                          925
Gly Gln Ala Met Cys Leu Ile Val Tyr Met Met Val Met Val Ile Gly
           935
                                      940
Asn Leu Val Val Leu Asn Leu Phe Leu Ala Leu Leu Leu Ser Ser Phe
945
             950
                                  955
Ser Ser Asp Asn Leu Thr Ala Ile Glu Glu Asp Pro Asp Ala Asn Asn
                                               975
              965
                              970
Leu Gln Ile Ala Val Thr Arg Ile Lys Lys Gly Ile Asn Tyr Val Lys
         980
                          985
                                           990
Gln Thr Leu Arg Glu Phe Ile Leu Lys Ala Phe Ser Lys Lys Pro Lys
      995
                       1000
                                1005
Ile Ser Arg Glu Ile Arg Gln Ala Glu Asp Leu Asn Thr Lys Lys Glu
                    1015
                               1020
Asn Tyr Ile Ser Asn His Thr Leu Ala Glu Met Ser Lys Gly His Asn
              1030 1035
                                                     1040
Phe Leu Lys Glu Lys Asp Lys Ile Ser Gly Phe Gly Ser Ser Val Asp
           1045 1050
                                                  1055
Lys His Leu Met Glu Asp Ser Asp Gly Gln Ser Phe Ile His Asn Pro
         1060
                           1065
                                             1070
Ser Leu Thr Val Thr Val Pro Ile Ala Pro Gly Glu Ser Asp Leu Glu
  1075 1080
                                          1085
Asn Met Asn Ala Glu Glu Leu Ser Ser Asp Ser Asp Ser Glu Tyr Ser
                   1095
                          1100
Lys Val Arg Leu Asn Arg Ser Ser Ser Ser Glu Cys Ser Thr Val Asp
1105 1110 1115 112
                                  1115
Asn Pro Leu Pro Gly Glu Gly Glu Ala Glu Ala Glu Pro Met Asn
             1125
                              1130
Ser Asp Glu Pro Glu Ala Cys Phe Thr Asp Gly Cys Val Arg Arg Phe
        1140
                         1145
                                             1150
Ser Cys Cys Gln Val Asn Ile Glu Ser Gly Lys Gly Lys Ile Trp Trp
     1155 1160
                                         1165
Asn Ile Arg Lys Thr Cys Tyr Lys Ile Val Glu His Ser Trp Phe Glu
   1170
                     1175
                                      1180
Ser Phe Ile Val Leu Met Ile Leu Leu Ser Ser Gly Ala Leu Ala Phe
                 1190
                                   1195
Glu Asp Ile Tyr Ile Glu Arg Lys Lys Thr Ile Lys Ile Ile Leu Glu
             1205
                              1210
Tyr Ala Asp Lys Ile Phe Thr Tyr Ile Phe Ile Leu Glu Met Leu Leu
          1220
                          1225 1230
Lys Trp Ile Ala Tyr Gly Tyr Lys Thr Tyr Phe Thr Asn Ala Trp Cys
                       1240
                                         1245
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Trp Leu Asp Phe Leu Ile Val Asp Val Ser Leu Val Thr Leu Val Ala 1250 1255 1260 Asn Thr Leu Gly Tyr Ser Asp Leu Gly Pro Ile Lys Ser Leu Arg Thr 1270 1275 Leu Arg Ala Leu Arg Pro Leu Arg Ala Leu Ser Arg Phe Glu Gly Met 1285 1290 1295 Arg Val Val Val Asn Ala Leu Ile Gly Ala Ile Pro Ser Ile Met Asn 1300 1305 1310 Val Leu Leu Val Cys Leu Ile Phe Trp Leu Ile Phe Ser Ile Met Gly 1315 1325 1320 Val Asn Leu Phe Ala Gly Lys Phe Tyr Glu Cys Ile Asn Thr Thr Asp 1330 1335 1340 Gly Ser Arg Phe Pro Ala Ser Gln Val Pro Asn Arg Ser Glu Cys Phe 1345 1350 1355 Ala Leu Met Asn Val Ser Gln Asn Val Arg Trp Lys Asn Leu Lys Val 1365 1370 Asn Phe Asp Asn Val Gly Leu Gly Tyr Leu Ser Leu Leu Gln Val Ala 1380 1385 1390 Thr Phe Lys Gly Trp Thr Ile Ile Met Tyr Ala Ala Val Asp Ser Val 1395 1400 1405 Asn Val Asp Lys Gln Pro Lys Tyr Glu Tyr Ser Leu Tyr Met Tyr Ile 1410 1415 1420 Tyr Phe Val Val Phe Ile Ile Phe Gly Ser Phe Phe Thr Leu Asn Leu 1430 1435 1440 Phe Ile Gly Val Ile Ile Asp Asn Phe Asn Gln Gln Lys Lys Leu 1445 1450 1455 Gly Gly Gln Asp Ile Phe Met Thr Glu Glu Gln Lys Lys Tyr Tyr Asn 1460 1465 1470 Ala Met Lys Lys Leu Gly Ser Lys Lys Pro Gln Lys Pro Ile Pro Arg 1475 1480 1485 Pro Gly Asn Lys Ile Gln Gly Cys Ile Phe Asp Leu Val Thr Asn Gln 1490 1495 1500 Ala Phe Asp Ile Ser Ile Met Val Leu Ile Cys Leu Asn Met Val Thr 1510 1515 Met Met Val Glu Lys Glu Gly Gln Ser Gln His Met Thr Glu Val Leu 1525 1530 1535 Tyr Trp Ile Asn Val Val Phe Ile Ile Leu Phe Thr Gly Glu Cys Val 1540 1545 1550 Leu Lys Leu Ile Ser Leu Arg His Tyr Tyr Phe Thr Val Gly Trp Asn 1555 1560 1565 Ile Phe Asp Phe Val Val Val Ile Ile Ser Ile Val Gly Met Phe Leu 1575 1580 Ala Asp Leu Ile Glu Thr Tyr Phe Val Ser Pro Thr Leu Phe Arg Val 1585 1590 1595 Ile Arg Leu Ala Arg Ile Gly Arg Ile Leu Arg Leu Val Lys Gly Ala 1605 1610 1615 Lys Gly Ile Arg Thr Leu Leu Phe Ala Leu Met Met Ser Leu Pro Ala 1620 1625 1630 Leu Phe Asn Ile Gly Leu Leu Leu Phe Leu Val Met Phe Ile Tyr Ala 1645 1635 1640 Ile Phe Gly Met Ser Asn Phe Ala Tyr Val Lys Lys Glu Asp Gly Ile 1655 1660 Asn Asp Met Phe Asn Phe Glu Thr Phe Gly Asn Ser Met Ile Cys Leu 1670 1675 Phe Gln Ile Thr Thr Ser Ala Gly Trp Asp Gly Leu Leu Ala Pro Ile 1685 1690

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Leu Asn Ser Lys Pro Pro Asp Cys Asp Pro Lys Lys Val His Pro Gly
      1700 1705 1710
Ser Ser Val Glu Gly Asp Cys Gly Asn Pro Ser Val Gly Ile Phe Tyr
   1715
                   1720
                                    1725
Phe Val Ser Tyr Ile Ile Ile Ser Phe Leu Val Val Val Asn Met Tyr
 1730
                 1735
                               1740
Ile Ala Val Ile Leu Glu Asn Phe Ser Val Ala Thr Glu Glu Ser Thr
1745 1750 1755 1760
Glu Pro Leu Ser Glu Asp Asp Phe Glu Met Phe Tyr Glu Val Trp Glu
       1765 1770 1775
Lys Phe Asp Pro Asp Ala Thr Gln Phe Ile Glu Phe Ser Lys Leu Ser
        1780 1785 1790
Asp Phe Ala Ala Ala Leu Asp Pro Pro Leu Leu Ile Ala Lys Pro Asn
1795 1800 1805
Lys Val Gln Leu Ile Ala Met Asp Leu Pro Met Val Ser Gly Asp Arg
 1810 1815 1820
Ile His Cys Leu Asp Ile Leu Phe Ala Phe Thr Lys Arg Val Leu Gly 1825 1830 1835 1840
                                          1840
Glu Ser Gly Glu Met Asp Ser Leu Arg Ser Gln Met Glu Glu Arg Phe
        1845 1850 1855
Met Ser Ala Asn Pro Ser Lys Val Ser Tyr Glu Pro Ile Thr Thr
        1860 1865
                            .
1870
Leu Lys Arg Lys Gln Glu Asp Val Ser Ala Thr Val Ile Gln Arg Ala
     1875 1880 1885
Tyr Arg Arg Tyr Arg Leu Arg Gln Asn Val Lys Asn Ile Ser Ser Ile
  1890 1895 1900
Tyr Ile Lys Asp Gly Asp Arg Asp Asp Leu Leu Asn Lys Lys Asp
      1910 1915
Met Ala Phe Asp Asn Val Asn Glu Asn Ser Ser Pro Glu Lys Thr Asp
      1925 1930
                                        1935
Ala Thr Ser Ser Thr Thr Ser Pro Pro Ser Tyr Asp Ser Val Thr Lys
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                       1945
                                    1950
Pro Asp Lys Glu Lys Tyr Glu Gln Asp Arg Thr Glu Lys Glu Asp Lys
    1955 1960
Gly Lys Asp Ser Lys Glu Ser Lys Lys
  1970
                1975
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Ile Phe Arg Phe Asn Ala Thr Pro Ala Leu Tyr Met Leu Ser Pro Phe
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Ser Pro Leu Arg Arg Ile Ser Ile Lys Ile Leu Val His Ser Leu Phe
                         120
                                           125
Ser Met Leu Ile Met Cys Thr Ile Leu Thr Asn Cys Ile Phe Met Thr
                      135
                                         140
Met Asn Asn Pro Pro Asp Trp Thr Lys Asn Val Glu Tyr Thr Phe Thr
     150
                                     155
Gly Ile Tyr Thr Phe Glu Ser Leu Val Lys Ile Leu Ala Arg Gly Phe
           165
                          170
                                          175
Cys Val Gly Glu Phe Thr Phe Leu Arg Asp Pro Trp Asn Trp Leu Asp 180 185 190
Phe Val Val Ile Val Phe Ala Tyr Leu Thr Glu Phe Val Asn Leu Gly
                          200
                                           205
Asn Val Ser Ala Leu Arg Thr Phe Arg Val Leu Arg Ala Leu Lys Thr
                      215
                                         220
Ile Ser Val Ile Pro Gly Leu Lys Thr Ile Val Gly Ala Leu Ile Gln
                230
                                   235
Ser Val Lys Lys Leu Ser Asp Val Met Ile Leu Thr Val Phe Cys Leu
245 250 255
               245
                                  250
Ser Val Phe Ala Leu Ile Gly Leu Gln Leu Phe Met Gly Asn Leu Lys
         260
                              265
His Lys Cys Phe Arg Asn Ser Leu Glu Asn Asn Glu Thr Leu Glu Ser
       275
                          280
Ile Met Asn Thr Leu Glu Ser Glu Glu Asp Phe Arg Lys Tyr Phe Tyr
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                                         300
Tyr Leu Glu Gly Ser Lys Asp Ala Leu Leu Cys Gly Phe Ser Thr Asp
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Ser Gly Gln Cys Pro Glu Gly Tyr Thr Cys Val Lys Ile Gly Arg Asn
325 330 335
Pro Asp Tyr Gly Tyr Thr Ser Phe Asp Thr Phe Ser Trp Ala Phe Leu
          340
                             345
                                                 350
Ala Leu Phe Arg Leu Met Thr Gln Asp Tyr Trp Glu Asn Leu Tyr Gln
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                         360
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Gln Thr Leu Arg Ala Ala Gly Lys Thr Tyr Met Ile Phe Phe Val Val
   370 375
                                         380
Val Ile Phe Leu Gly Ser Phe Tyr Leu Ile Asn Leu Ile Leu Ala Val
                  390
                                    395
Val Ala Met Ala Tyr Glu Glu Gln Asn Gln Ala Asn Ile Glu Glu Ala
              405
                                  410
Lys Gln Lys Glu Leu Glu Phe Gln Gln Met Leu Asp Arg Leu Lys Lys
          420
                              425
Glu Gln Glu Glu Ala Glu Ala Ile Ala Ala Ala Ala Ala Glu Tyr Thr
      435
                          440
                                             445
Ser Ile Arg Arg Ser Arg Ile Met Gly Leu Ser Glu Ser Ser Glu
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                    455
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Thr Ser Lys Leu Ser Ser Lys Ser Ala Lys Glu Arg Arg Asn Arg Arg 465 470 475 480
Lys Lys Lys Asn Gln Lys Lys Leu Ser Ser Gly Glu Glu Lys Gly Asp
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                                 490
Ala Glu Lys Leu Ser Lys Ser Glu Ser Glu Asp Ser Ile Arg Arg Lys
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Ser Phe His Leu Gly Val Glu Gly His Arg Arg Ala His Glu Lys Arg
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Leu Ser Thr Pro Asn Gln Ser Pro Leu Ser Ile Arg Gly Ser Leu Phe
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Ser Ala Arg Arg Ser Ser Arg Thr Ser Leu Phe Ser Phe Lys Gly Arg
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Gly Arg Asp Ile Gly Ser Glu Thr Glu Phe Ala Asp Asp Glu His Ser
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                                 570
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Ile Phe Gly Asp Asn Glu Ser Arg Arg Gly Ser Leu Phe Val Pro His
           580
                 585
                                                 590
Arg Pro Gln Glu Arg Arg Ser Ser Asn Ile Ser Gln Ala Ser Arg Ser
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                                             605
Pro Pro Met Leu Pro Val Asn Gly Lys Met His Ser Ala Val Asp Cys
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Asn Gly Val Val Ser Leu Val Asp Gly Arg Ser Ala Leu Met Leu Pro
625
                   630
                                      635
Asn Gly Gln Leu Leu Pro Glu Gly Thr Thr Asn Gln Ile His Lys Lys
               645
                                650
Arg Arg Cys Ser Ser Tyr Leu Leu Ser Glu Asp Met Leu Asn Asp Pro
           660
                             665
                                                  670
Asn Leu Arg Gln Arg Ala Met Ser Arg Ala Ser Ile Leu Thr Asn Thr
                    680
                                             685
Val Glu Glu Leu Glu Glu Ser Arg Gln Lys Cys Pro Pro Trp Trp Tyr
                     695
                                          700
Arg Phe Ala His Lys Phe Leu Ile Trp Asn Cys Ser Pro Tyr Trp Ile
                 710
                                   715
Lys Phe Lys Lys Cys Ile Tyr Phe Ile Val Met Asp Pro Phe Val Asp
               725
                                 730
Leu Ala Val Thr Ile Cys Ile Val Leu Asn Thr Leu Phe Met Ala Met
         740
                              745
Glu His His Pro Met Thr Glu Glu Phe Lys Asn Val Leu Ala Ile Gly
       755
                          760
                                             765
Asn Leu Val Phe Thr Gly Ile Phe Ala Ala Glu Met Val Leu Lys Leu
                       775
                                          780
Ile Ala Met Asp Pro Tyr Glu Tyr Phe Gln Val Gly Trp Asn Ile Phe
                  790
                                   795
Asp Ser Leu Ile Val Thr Leu Ser Leu Val Glu Leu Phe Leu Ala Asp
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                                 810
                                                     815
Val Glu Gly Leu Ser Val Leu Arg Ser Phe Arg Leu Leu Arg Val Phe
          820
                             825
                                                830
Lys Leu Ala Lys Ser Trp Pro Thr Leu Asn Met Leu Ile Lys Ile Ile
835 840 845
                         840
                                             845
Gly Asn Ser Val Gly Ala Leu Gly Asn Leu Thr Leu Val Leu Ala Ile
                     855
Ile Val Phe Ile Phe Ala Val Val Gly Met Gln Leu Phe Gly Lys Ser
                  870
                                     875
Tyr Lys Glu Cys Val Cys Lys Ile Asn Asp Asp Cys Thr Leu Pro Arg
              885
                                 890
Trp His Met Asn Asp Phe Phe His Ser Phe Leu Ile Val Phe Arg Val
          900
                              905
                                                910
Leu Cys Gly Glu Trp Ile Glu Thr Met Trp Asp Cys Met Glu Val Ala
915 920 925
Gly Gln Ala Met Cys Leu Ile Val Tyr Met Met Val Met Val Ile Gly
                     935
                                          940
Asn Leu Val Val Leu Asn Leu Phe Leu Ala Leu Leu Leu Ser Ser Phe
               950
                                     955
Ser Ser Asp Asn Leu Thr Ala Ile Glu Glu Asp Pro Asp Ala Asn Asn
           965
                                970
Leu Gln Ile Ala Val Thr Arg Ile Lys Lys Gly Ile Asn Tyr Val Lys
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980
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Gln Thr Leu Arg Glu Phe Ile Leu Lys Ala Phe Ser Lys Lys Pro Lys
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Ile Ser Arg Glu Ile Arg Gln Ala Glu Asp Leu Asn Thr Lys Lys Glu
                   1015 1020
Asn Tyr Ile Ser Asn His Thr Leu Ala Glu Met Ser Lys Gly His Asn
       1030 1035
Phe Leu Lys Glu Lys Asp Lys Ile Ser Gly Phe Gly Ser Ser Val Asp
     1045 1050 1055
Lys His Leu Met Glu Asp Ser Asp Gly Gln Ser Phe Ile His Asn Pro
       1060 1065 1070
Ser Leu Thr Val Thr Val Pro Ile Ala Pro Gly Glu Ser Asp Leu Glu
      1075
                      1080
                             1085
Asn Met Asn Ala Glu Glu Leu Ser Ser Asp Ser Asp Ser Glu Tyr Ser
  1090
                  1095 1100
Lys Val Arg Leu Asn Arg Ser Ser Ser Ser Glu Cys Ser Thr Val Asp
         1110 1115
Asn Pro Leu Pro Gly Glu Gly Glu Glu Ala Glu Ala Glu Pro Met Asn
           1125 1130
                                             1135
Ser Asp Glu Pro Glu Ala Cys Phe Thr Asp Gly Cys Val Arg Arg Phe
        1140 1145 1150
Ser Cys Cys Gln Val Asn Ile Glu Ser Gly Lys Gly Lys Ile Trp Trp 1155 1160 1165
Asn Ile Arg Lys Thr Cys Tyr Lys Ile Val Glu His Ser Trp Phe Glu
 1170 1175
                                  1180
Ser Phe Ile Val Leu Met Ile Leu Leu Ser Ser Gly Ala Leu Ala Phe
1185
       1190 1195
Glu Asp Ile Tyr Ile Glu Arg Lys Lys Thr Ile Lys Ile Ile Leu Glu
            1205 1210 1215
Tyr Ala Asp Lys Ile Phe Thr Tyr Ile Phe Ile Leu Glu Met Leu Leu 1220 1225 1230
Lys Trp Ile Ala Tyr Gly Tyr Lys Thr Tyr Phe Thr Asn Ala Trp Cys
                     1240 1245
Trp Leu Asp Phe Leu Ile Val Asp Val Ser Leu Val Thr Leu Val Ala
   1250 1255 1260
Asn Thr Leu Gly Tyr Ser Asp Leu Gly Pro Ile Lys Ser Leu Arg Thr
1265 1270 1275
Leu Arg Ala Leu Arg Pro Leu Arg Ala Leu Ser Arg Phe Glu Gly Met
            1285 1290
Arg Val Val Asn Ala Leu Ile Gly Ala Ile Pro Ser Ile Met Asn 1300 1305 1310
Val Leu Leu Val Cys Leu Ile Phe Trp Leu Ile Phe Ser Ile Met Gly
     1315
                     1320
                                     1325
Val Asn Leu Phe Ala Gly Lys Phe Tyr Glu Cys Ile Asn Thr Thr Asp
  1330 1335
                           1340
Gly Ser Arg Phe Pro Ala Ser Gln Val Pro Asn Arg Ser Glu Cys Phe
        1350 1355
Ala Leu Met Asn Val Ser Gln Asn Val Arg Trp Lys Asn Leu Lys Val
1365 1370 1375
Asn Phe Asp Asn Val Gly Leu Gly Tyr Leu Ser Leu Leu Gln Val Ala
1380 1385 1390
Thr Phe Lys Gly Trp Thr Ile Ile Met Tyr Ala Ala Val Asp Ser Val
     1395 1400
Asn Val Asp Lys Gln Pro Lys Tyr Glu Tyr Ser Leu Tyr Met Tyr Ile
1410 1415 1420
Tyr Phe Val Val Phe Ile Ile Phe Gly Ser Phe Phe Thr Leu Asn Leu
```

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                              1435
Phe Ile Gly Val Ile Ile Asp Asn Phe Asn Gln Gln Lys Lys Leu
            1445 1450
                                1455
Gly Gly Gln Asp Ile Phe Met Thr Glu Glu Gln Lys Lys Tyr Tyr Asn
        1460 1465 1470
Ala Met Lys Lys Leu Gly Ser Lys Lys Pro Gln Lys Pro Ile Pro Arg
      1475
           1480 1485
Pro Gly Asn Lys Ile Gln Gly Cys Ile Phe Asp Leu Val Thr Asn Gln
  1490 1495 1500
Ala Phe Asp Ile Ser Ile Met Val Leu Ile Cys Leu Asn Met Val Thr
1505 1510 1515 1520
Met Met Val Glu Lys Glu Gly Gln Ser Gln His Met Thr Glu Val Leu
           1525
                           1530
Tyr Trp Ile Asn Val Val Phe Ile Ile Leu Phe Thr Gly Glu Cys Val
        1540
                       1545
                                       1550
Leu Lys Leu Ile Ser Leu Arg His Tyr Tyr Phe Thr Val Gly Trp Asn
1555 1560 1565
Ile Phe Asp Phe Val Val Val Ile Ile Ser Ile Val Gly Met Phe Leu
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Lys Gly Ile Arg Thr Leu Leu Phe Ala Leu Met Met Ser Leu Pro Ala
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Leu Phe Asn Ile Gly Leu Leu Phe Leu Val Met Phe Ile Tyr Ala
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Asn Asp Met Phe Asn Phe Glu Thr Phe Gly Asn Ser Met Ile Cys Leu
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Phe Gln Ile Thr Thr Ser Ala Gly Trp Asp Gly Leu Leu Ala Pro Ile
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                         1690 1695
Leu Asn Ser Lys Pro Pro Asp Cys Asp Pro Lys Lys Val His Pro Gly
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Ser Ser Val Glu Gly Asp Cys Gly Asn Pro Ser Val Gly Ile Phe Tyr
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Phe Val Ser Tyr Ile Ile Ile Ser Phe Leu Val Val Asn Met Tyr
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          1735 1740
Ile Ala Val Ile Leu Glu Asn Phe Ser Val Ala Thr Glu Glu Ser Thr
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Glu Pro Leu Ser Glu Asp Asp Phe Glu Met Phe Tyr Glu Val Trp Glu
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                          1770
Lys Phe Asp Pro Asp Ala Thr Gln Phe Ile Glu Phe Ser Lys Leu Ser
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                                1820
Ile His Cys Leu Asp Ile Leu Phe Ala Phe Thr Lys Arg Val Leu Gly
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Glu Ser Gly Glu Met Asp Ser Leu Arg Ser Gln Met Glu Glu Arg Phe
          1845 1850
Met Ser Ala Asn Pro Ser Lys Val Ser Tyr Glu Pro Ile Thr Thr Thr 1860 1865 1870
Leu Lys Arg Lys Gln Glu Asp Val Ser Ala Thr Val Ile Gln Arg Ala
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1890 1895 1900

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1905 1910 1915 1920

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1925 1930 1930

Ala Thr Ser Ser Thr Thr Ser Pro Pro Ser Tyr Asp Ser Val Thr Lys
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1610

1615

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Leu Asn Ser Lys Pro Pro Asp Cys Asp Pro Lys Lys Val His Pro Gly 1700 1705 1710
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	crrrorar bequence				
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100 105 110 105 Ser Pro Leu Arg Arg Ile Ser Ile Lys Ile Leu Val His Ser Leu Phe 115 120 125 Ser Met Leu Ile Met Cys Thr Ile Leu Thr Asn Cys Ile Phe Met Thr 135 140 Met Asn Asn Pro Pro Asp Trp Thr Lys Asn Val Glu Tyr Thr Phe Thr 150 155 Gly Ile Tyr Thr Phe Glu Ser Leu Val Lys Ile Leu Ala Arg Gly Phe 165 170 175 Cys Val Gly Glu Phe Thr Phe Leu Arg Asp Pro Trp Asn Trp Leu Asp 180 185 190 Phe Val Val Ile Val Phe Ala Tyr Leu Thr Glu Phe Val Asn Leu Gly 200 205 Asn Val Ser Ala Leu Arg Thr Phe Arg Val Leu Arg Ala Leu Lys Thr 215 220 Ile Ser Val Ile Pro Gly Leu Lys Thr Ile Val Gly Ala Leu Ile Gln 230 235 Ser Val Lys Lys Leu Ser Asp Val Met Ile Leu Thr Val Phe Cys Leu
245 250 255 245 250 Ser Val Phe Ala Leu Ile Gly Leu Gln Leu Phe Met Gly Asn Leu Lys 260 265 His Lys Cys Phe Arg Asn Ser Leu Glu Asn Asn Glu Thr Leu Glu Ser 275 280 285 Ile Met Asn Thr Leu Glu Ser Glu Glu Asp Phe Arg Lys Tyr Phe Tyr 290 295 300 Tyr Leu Glu Gly Ser Lys Asp Ala Leu Leu Cys Gly Phe Ser Thr Asp 305 310 315 320 Ser Gly Gln Cys Pro Glu Gly Tyr Thr Cys Val Lys Ile Gly Arg Asn 325 330 335 Ala Leu Phe Arg Leu Met Thr Gln Asp Tyr Trp Glu Asn Leu Tyr Gln 355 360 Gln Thr Leu Arg Ala Ala Gly Lys Thr Tyr Met Ile Phe Phe Val Val 375 380 Val Ile Phe Leu Gly Ser Phe Tyr Leu Ile Asn Leu Ile Leu Ala Val

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Lys Gln Lys Glu Leu Glu Phe Gln Gln Met Leu Asp Arg Leu Lys Lys
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                             425
                                                 430
Glu Gln Glu Glu Ala Glu Ala Ile Ala Ala Ala Ala Glu Tyr Thr
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                                            445
Ser Ile Arg Arg Ser Arg Ile Met Gly Leu Ser Glu Ser Ser Ser Glu
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Thr Ser Lys Leu Ser Ser Lys Ser Ala Lys Glu Arg Arg Asn Arg Arg
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Lys Lys Lys Asn Gln Lys Lys Leu Ser Ser Gly Glu Glu Lys Gly Asp
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Ala Glu Lys Leu Ser Lys Ser Glu Ser Glu Asp Ser Ile Arg Arg Lys
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Ser Ala Arg Arg Ser Ser Arg Thr Ser Leu Phe Ser Phe Lys Gly Arg
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Gly Arg Asp Ile Gly Ser Glu Thr Glu Phe Ala Asp Asp Glu His Ser
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Ile Phe Gly Asp Asn Glu Ser Arg Arg Gly Ser Leu Phe Val Pro His
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Arg Pro Gln Glu Arg Arg Ser Ser Asn Ile Ser Gln Ala Ser Arg Ser
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Arg Arg Cys Ser Ser Tyr Leu Leu Ser Glu Asp Met Leu Asn Asp Pro
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Lys Phe Lys Lys Cys Ile Tyr Phe Ile Val Met Asp Pro Phe Val Asp
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Leu Ala Ile Thr Ile Cys Ile Val Leu Asn Thr Leu Phe Met Ala Met
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Glu His His Pro Met Thr Glu Glu Phe Lys Asn Val Leu Ala Ile Gly
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Asn Leu Val Phe Thr Gly Ile Phe Ala Ala Glu Met Val Leu Lys Leu
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Ile Ala Met Asp Pro Tyr Glu Tyr Phe Gln Val Gly Trp Asn Ile Phe
              790
                                     795
Asp Ser Leu Ile Val Thr Leu Ser Leu Val Glu Leu Phe Leu Ala Asp
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                                 810
Val Glu Gly Leu Ser Val Leu Arg Ser Phe Arg Leu Leu Arg Val Phe
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Lys Leu Ala Lys Ser Trp Pro Thr Leu Asn Met Leu Ile Lys Ile Ile
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Tyr Lys Glu Cys Val Cys Lys Ile Asn Asp Asp Cys Thr Leu Pro Arg
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                  890
                                             895
Trp His Met Asn Asp Phe Phe His Ser Phe Leu Ile Val Phe Arg Val
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                         905
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Leu Cys Gly Glu Trp Ile Glu Thr Met Trp Asp Cys Met Glu Val Ala
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Gly Gln Ala Met Cys Leu Ile Val Tyr Met Met Val Met Val Ile Gly
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Asn Leu Val Val Leu Asn Leu Phe Leu Ala Leu Leu Ser Ser Phe
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Ser Ser Asp Asn Leu Thr Ala Ile Glu Glu Asp Pro Asp Ala Asn Asn
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Leu Gln Ile Ala Val Thr Arg Ile Lys Lys Gly Ile Asn Tyr Val Lys
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Gln Thr Leu Arg Glu Phe Ile Leu Lys Ala Phe Ser Lys Lys Pro Lys
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                     1000
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Asn Tyr Ile Ser Asn His Thr Leu Ala Glu Met Ser Lys Gly His Asn
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Phe Leu Lys Glu Lys Asp Lys Ile Ser Gly Phe Gly Ser Ser Val Asp
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Lys His Leu Met Glu Asp Ser Asp Gly Gln Ser Phe Ile His Asn Pro
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Ser Leu Thr Val Thr Val Pro Ile Ala Pro Gly Glu Ser Asp Leu Glu
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      1075
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Asn Met Asn Ala Glu Glu Leu Ser Ser Asp Ser Asp Ser Glu Tyr Ser
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Lys Val Arg Leu Asn Arg Ser Ser Ser Ser Glu Cys Ser Thr Val Asp
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Asn Pro Leu Pro Gly Glu Gly Glu Ala Glu Ala Glu Pro Met Asn
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Ser Asp Glu Pro Glu Ala Cys Phe Thr Asp Gly Cys Val Arg Arg Phe
                1145 1150
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Ser Cys Cys Gln Val Asn Ile Glu Ser Gly Lys Gly Lys Ile Trp Trp
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Asn Ile Arg Lys Thr Cys Tyr Lys Ile Val Glu His Ser Trp Phe Glu
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Tyr Ala Asp Lys Ile Phe Thr Tyr Ile Phe Ile Leu Glu Met Leu Leu
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Lys Trp Ile Ala Tyr Gly Tyr Lys Thr Tyr Phe Thr Asn Ala Trp Cys
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Trp Leu Asp Phe Leu Ile Val Asp Val Ser Leu Val Thr Leu Val Ala
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Leu Arg Ala Leu Arg Pro Leu Arg Ala Leu Ser Arg Phe Glu Gly Met
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Gly Ser Arg Phe Pro Ala Ser Gln Val Pro Asn Arg Ser Glu Cys Phe
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Ala Leu Met Asn Val Ser Gln Asn Val Arg Trp Lys Asn Leu Lys Val
       1365 1370 1375
Asn Phe Asp Asn Val Gly Leu Gly Tyr Leu Ser Leu Leu Gln Val Ala
1380 1385 1390
Thr Phe Lys Gly Trp Thr Ile Ile Met Tyr Ala Ala Val Asp Ser Val
      1395 1400 1405
Asn Val Asp Lys Gln Pro Lys Tyr Glu Tyr Ser Leu Tyr Met Tyr Ile
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Tyr Phe Val Val Phe Ile Ile Phe Gly Ser Phe Phe Thr Leu Asn Leu
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Phe Ile Gly Val Ile Ile Asp Asn Phe Asn Gln Gln Lys Lys Lys Leu
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Ala Met Lys Lys Leu Gly Ser Lys Lys Pro Gln Lys Pro Ile Pro Arg
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Pro Gly Asn Lys Ile Gln Gly Cys Ile Phe Asp Leu Val Thr Asn Gln
1490 1495 1500
Ala Phe Asp Ile Ser Ile Met Val Leu Ile Cys Leu Asn Met Val Thr
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Met Met Val Glu Lys Glu Gly Gln Ser Gln His Met Thr Glu Val Leu
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Tyr Trp Ile Asn Val Val Phe Ile Ile Leu Phe Thr Gly Glu Cys Val
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Leu Lys Leu Ile Ser Leu Arg His Tyr Tyr Phe Thr Val Gly Trp Asn
     1555 1560
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Ile Phe Asp Phe Val Val Ile Ile Ser Ile Val Gly Met Phe Leu
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Lys Gly Ile Arg Thr Leu Leu Phe Ala Leu Met Met Ser Leu Pro Ala
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Leu Phe Asn Ile Gly Leu Leu Phe Leu Val Met Phe Ile Tyr Ala
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            1640 1645
Ile Phe Gly Met Ser Asn Phe Ala Tyr Val Lys Lys Glu Asp Gly Ile
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Phe Gln Ile Thr Thr Ser Ala Gly Trp Asp Gly Leu Leu Ala Pro Ile
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Leu Asn Ser Lys Pro Pro Asp Cys Asp Pro Lys Lys Val His Pro Gly
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Phe Val Ser Tyr Ile Ile Ile Ser Phe Leu Val Val Val Asn Met Tyr
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